Inadvertent Rapid Lipid Emulsion Administration

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Parenteral nutrition (PN) is indicated when nutritional requirements cannot be met via intestinal absorption. In most cases patients receive an intravenous (IV) solution containing fluids, electrolytes, micronutrients and macronutrients (amino acids and carbohydrates), as well as an intravenous lipid emulsion (ILE) – given as an all-in-one admixture solution or as a separate infusion. These solutions should be administered under strict dosage and infusion rates in order to avoid delivery that exceeds the maximal utilization rate of lipids.

When infusion rate and dosage exceed the maximal utilization rate, fat overload syndrome (FOS) may develop. FOS is usually an iatrogenic condition, caused mostly by the inadvertent administration of lipid-containing solutions at an excessive dosage. The syndrome has previously been reported to cause a wide range of symptoms including fever, elevations in liver enzymes, hepatosplenomegaly, coagulation disorders, leukopenia, thrombocytopenia, seizures, respiratory distress, and even death [1]. Care and treatment of these patients is mostly supportive, although in rare and severe cases plasma exchange may be considered.

The pathological mechanisms responsible for the clinical presentation include several pathways: mechanical engorgement and obstruction of capillaries, damage to the functional structure of vital organs such as the brain and kidneys, sedimentation in and disruption of platelet and white blood cell function, and endothelial injury causing inflammatory and fibrinolytic reactions due to release of active proteins such as tissue plasminogen activator [2].

In this case report we both emphasize the significance and risk of FOS, and describe the risk-management process performed in one tertiary pediatric center following a case of lipid overdose, in order to highlight the importance of the risk inherent in IV administration of PN.

PATIENT DESCRIPTION

A 6-month-old male infant with Griscelli syndrome (an autosomal recessive syndrome that features hypopigmentation and may include immunodeficiency and neurologic deficits) presented with vomiting and diarrhea 2 months after allogeneic bone marrow transplantation. At presentation to the Emergency Department he was tachycardic (145 beats/min) but normotensive (85/48 mmHg), alert, and in good general condition. His weight was 7.04 kg and his height 64 cm. Physical examination revealed a known hepatosplenomegaly, stable compared to prior examinations. Initial blood work showed lymphopenia, low yet stable hemoglobin, elevated urea but normal creatinine, no electrolyte disturbances, normal C-reactive protein (CRP), normal blood gases, and normal urinalysis. Abdominal radiography was normal.

On the second day of hospitalization, after assessment of his nutritional status and anticipation of long-term PN need, with concomitant inability to tolerate feedings via nasogastric tube, the infant started receiving PN with a lipid solution (Lipofundin® 20%, B. Braun Melsungen AG, Germany) containing an equal mixture of soy oil and medium chain triglycerides (MCT). On the fifth day of hospitalization, he underwent sigmoidoscopy owing to suspected intestinal manifestations of graft-versus-host disease, during which he was disconnected from his PN and ILE solutions. On returning to the pediatric ward, he was reconnected to the IV pumps (lipids provided separately) and administration of the solutions was resumed.

Later that evening the team discovered that the infant had received the ILE solution at a higher set rate, using the pump formerly used for PN administration. The infant received an excess rate of 38 ml/hr (5.4 ml/kg/hr) Lipofundin 20% emulsion for 3.5 hours (10 times the maximal daily amount). On-site investigation revealed that both the PN solution and the ILE were given in identical pumps, and during the reconnection the two solutions were switched with ILE given at the rate of the amino acid standard solution and vice versa. When the error in administration was detected, the infusion was stopped, vital signs and a complete physical examination were performed, blood work was taken, and the infant was transferred for observation to the Pediatric Intensive Care Unit (PICU). The child was in good condition upon discovery of the dosage error, with normal vital signs. Laboratory workup showed significant hypertriglyceridemia (6417 md/dl) with normal cholesterol levels, lymphopenia (0.1 K/μl) with elevated hemoglobin (20 g/dl), mild hypokalemia (3.0 mEq/L), hypomagnesemia (1.36 mg/dl), normal liver enzyme levels and kidney function tests, normal clotting functions with low fibrinogen levels (135 mg/dl), and no elevation in CRP.

The child remained in the PICU for about 24 hours, with no significant change in his condition and no report of new symptoms or clinical signs. Under supportive care, without plasmapheresis, triglyceride levels and other abnormalities normalized during the first 24 hours after the lipid

overdose, apart from those related to his underlying medical condition (lymphopenia, low fibrinogen levels). His hospitalization continued in the oncology ward, with no further known complication of the lipid overdose. Laboratory data during the hospitalization are shown in Table 1.

COMMENT

In this report we describe the inadvertent administration of intravenous lipid solution to a 6-month-old child, which led to significant hypertriglyceridemia with no accompanying symptoms or long-lasting medical harm.

In the past, ILEs comprised mainly soybean-based solution, rich with omega-6 fatty acids (Intralipid® 20%, Baxter Healthcare Corporation, USA). The composition of these emulsions may be responsible for PN-associated complications such as increased oxidation, reduced lipid turnover, hepatotoxicity, and sepsis [3].

Since the early 1990s there has been an increase in the use of ILEs containing other sources of lipids, including olive oil and MCTs. Since 2004, fish oil-based lipid emulsions rich in omega-3 fatty acids (Omegaven, SMOF-lipid) were introduced. Case series that studied children exposed to high dosages of these solutions showed no significant clinical effects apart from transitory elevation of liver enzymes [1]. Earlier research demonstrated that long-term consumption of omega-3 fatty acids caused a decrease in postprandial triglyceride levels through the up-regulation of lipoprotein lipase activity, thereby contributing to a decrease in chylomicron size and half-life [4].

As with any administration of IV drugs, there are several technical weak points that might cause errors in dosage or rate of administration, endangering the health and wellbeing of the patient. In this case, we found that the critical error occurred when solutions were given simultaneously using similar-looking infusion pumps used at different rates of infusion. As stated earlier, ILE can be provided in a separate line or as part of an all-in-one admixture. Since our facility moved to the use of standard amino acid-based solutions, ILE must be given separately, emphasizing the need to avoid confusion in the use of the IV pumps. The hospital's risk management committee reviewed the case and ordered that ILE administration be given only through designated pumps, marked with a sticker warning against the use of an infusion rate higher than 1 ml/kg/hr (equivalent to 0.2 g fat per kg/hr). This rate was chosen both for ease of remembering and for being within the safe recommended range for ILE administration [3]. Furthermore, it was decided that autopumps and solutions will be checked three times during each nurse's shift.

This is the second report in the literature of hypertriglyceridemia following the administration of Lipofundin® ILE [5]. It shows, as does the previous report, that hypertriglyceridemia can still occur with new ILEs; that despite the advantages of standard PN solutions the reconnection of multiple pumps may be hazardous, and care should be given after proper marking and monitoring of the solutions. In addition, when triglyceride levels are above 5000 mg/dl but there are no coagulation abnormalities or systemic effects, observation without intervention can be practiced.

Table 1. Laboratory results during hospitalization (abnormal results in bold)

	Baseline values before TPN (1 Jan 2017)	During TPN treatment (-8 hrs) (5 March 2017, 11:02)	Immediately after cessation of drip (0 hrs) (5 March 2017, 19:01)	12 hrs after administration (5 March 2017, 06:30)	84 hrs after administration (9 March 2017, 07:00)
Sodium (132–140 mg/dl)	135	134	132	138	135
Potassium (4.1–5.3 mEq/L)	5.8	5.1	**3**	4.3	5.1
Phosphorus (4–6.5 mg/dl)	**5.3**	**3.8**	**1.9**	4	4.9
Magnesium (1.7–2.3 mg/dl)	2.48	2.05	**1.36**	1.81	2.27
LDH (0–975 U/L)	349	648	556	501	442
AST (15–60 U/L)	24.8	23.2	20.5	22.7	23.1
ALT (13–45 U/L)	60	17	18	19.3	19
Alkaline phosphatase (82–383 U/L)	98	268	285	272	210
GGT (12–122 U/L)	225	29	37	79	47
Triglycerides (< 150 mg/dl)	74	76	**6417**	**205**	132
Cholesterol (< 200 mg/dl)			**263**		**235**
WBC (6–18.5 K/µl)	2.20	**2.98**	9.52	**4.29**	**1.54**
ANC (1.5-8.5 K/µl)	0.7	2.1	9	3.5	**1.1**
Lymphocytes (3.3–11.8 K/µl)	1.4	**0.5**	**0.1**	**0.5**	**0.3**
Hb (9.5–13 g/dl)	12.3	13.7	20	12.5	11.3
Platelets (150–450 K/µl)	861	233	225	167	208
Fibrinogen (300–530 mg/dl)	258		**135**	**177**	

LDH = low-density lipoprotein, AST = aspartate aminotransferase, ALT = alanine aminotransferase, GGT = gamma-glutamyl transpeptidase, WBC = white blood cells, ABC = absolute neutrophil count, Hb = hemoglobin

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References

1. Gura KM, Puder M. Rapid infusion of fish oil-based emulsion in infants does not appear to be associated with fat overload syndrome. *Nutr Clin Pract* 2010; 25 (4): 399-402.
2. Haber LM, Hawkins EP, Seilheimer DK, Saleem A. Fat overload syndrome: an autopsy study with evaluation of the coagulopathy. *Am J Clin Pathol* 1988; 90 (2): 223-7.
3. Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R. Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr* 2005; 41 (Suppl 2): S1-87.
4. Park Y, Harris WS. Omega-3 fatty acid supplementation accelerates chylomicron triglyceride clearance. *J Lipid Res* 2003; 44 (3): 455-63.
5. Kolacek S, Hojsak I. Fat overload syndrome after the rapid infusion of SMOF lipid emulsion. *J Parenter Enteral Nutr* 2014; 38 (1): 119-21.